## REMARKS

### *Status of the Claims*

Claims 1-20 were pending in the present application. Claims 10 and 20 were withdrawn from consideration by the Examiner. By virtue of this response, claims 1, 8-10, and 19 have been amended, claims 7 and 18 have been cancelled, and new claims 21-26 have been added. Accordingly, claims 1-6, 8, 9, 11-17, 19, and 21-26 are currently under consideration.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

### *Interview Summary*

A telephonic interview with Examiner Saucier was held on February 28, 2007. In addition to Examiner Saucier and Alicia Hager (the undersigned), Gladys Monroy, and David Cook participated in the interview. Applicants and their representatives would again like to thank Examiner Saucier for the courtesy of the telephonic interview.

The subject of the telephonic interview was the Office Action dated November 24, 2006. Claims discussed included claims 1 and 6. Possible amendments to claim 1 were discussed. In addition, two references cited in the Office Action, Roth et al. and U.S. Patent No. 5,232,844, dated November 24, 2006, were discussed. Example 9 of Applicants' specification was also discussed during the interview.

### *Specification*

The disclosure is objected to because the continuity information for U.S. Patent Application No. 09/912,031 has not been updated. In response, we have amended paragraph [0001] of the specification to indicate U.S. Patent Application No. 09/912,031 has become U.S. Patent No. 6,709,810. No new matter is added.

***Information Disclosure Statement***

The Examiner has indicated that the listing of references on Form PTO/SB/08a/b for the Information Disclosure Statement filed October 5, 2006, was incomplete.

Reference 81 of the Information Disclosure Statement filed October 5, 2006, was identified as missing the date of publication. In response, Applicants submit the attached Supplemental Information Disclosure Statement containing the date of publication for this reference.

In addition, references 37, 45, 46, 80 and 94 of the Information Disclosure Statement filed October 5, 2006, could not be located by the Examiner in association with the parent applications. In response, Applicants submit the attached Supplemental Information Disclosure Statement containing copies of each of these references.

***Claim Amendments***

Claims 1, 8-10, and 19 have been amended by virtue of this Amendment.

Claim 1 is directed to a method of treating a material comprising red blood cells. Claim 1 has now been amended to more clearly indicate that the compound added to the material in order to inactivate a pathogen if present, inactivates at least about 1 log of the pathogen, if the pathogen is present in the material. Support for this amendment is found, e.g., in claim 1 as filed.

Claim 1 has also been amended to indicate that the compound that is added to the material comprising red blood cells in order to inactivate a pathogen, if present, comprises a nucleic acid binding ligand and a functional group which is, or which forms, the electrophilic group. Support for this amendment is found, e.g., in claims 7 and 18 as filed, as well as in lines 1-4 of paragraph [0016], paragraph [0036], lines 3-6 of paragraph [0047], and lines 10-14 of paragraph [0055] of the specification.

Claim 1 has been further amended to state that an effective amount of the quencher is added that reduces the level of side reactions of the compound in the material comprising red blood cells. Support for these amendments can be found in claim 1 as originally filed, as well as throughout the specification.

Claim 1 has also been amended to clarify that the nucleophilic group of the quencher reacts covalently with the electrophilic group of or formed by the pathogen-inactivating compound in the material and to indicate that the quencher reduces the level of side reactions of the compound in the material comprising red blood cells. Support for these amendments can be found in claim 1 as originally filed, as well as throughout the specification.

Thus, as amended, the method of claim 1 is a method of treating a material comprising red blood cells that comprises: a) adding a compound to the material comprising red blood cells in order to inactivate a pathogen, if present in the material, the compound comprising a nucleic acid binding ligand and a functional group which is, or which forms, an electrophilic group, wherein the electrophilic group can react covalently with nucleic acid; and b) adding an effective amount of a quencher to the material comprising red blood cells that reduces the level of side reactions of the compound, wherein the quencher comprises a nucleophilic group that reacts covalently with the electrophilic group, wherein the addition of the quencher is done prior to, simultaneously with, or within about 20 minutes after the addition of the compound, and wherein the compound inactivates at least about 1 log of the pathogen, if present in the material. Claims 2-6, 8, 9, 11-17, 19, and 21-25 all depend directly or indirectly from claim 1, and therefore incorporate all limitations of claim 1.

Claims 7 and 18 have been cancelled due to the amendment of claim 1.

The amendments made to claims 8, 10, and 19 are due to the amendment of claim 1 and cancellation of claims 7 and 18.

Claim 9 has now been amended to more clearly indicate that the compound added to the material in order to inactivate a pathogen if present, inactivates at least about 3 logs of the pathogen,

*if* the pathogen is present in the material. Support for this amendment is found, e.g., in line 4 of claim 1, as filed.

New claims 21-26 have been added by virtue of this Amendment. Support for new claims 21 and 23 is found, e.g., in lines 10-12 of paragraph [0018]. Support for new claims 22 and 24 is found, e.g., in paragraph [0017] and paragraph [0049]. Support for new claims 25 and 26 is found, e.g., in the last sentence of paragraph [0021], the last sentence of paragraph [0048], and paragraph [0069].

No new matter has been added by the claim amendments.

***Double Patenting***

*Double Patenting Rejection #1*

Claims 1-9 and 11-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-56 of U.S. Patent No. 6,270,952.

As indicated by the Examiner, the provisional obviousness-type double patenting rejection would be overcome by a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c). In the interest of expediting prosecution and without acquiescing as to the merits of the rejection, Applicants request submit that they will file a terminal disclaimer in the present application to disclaim any term beyond the term of U.S. Patent No. 6,270,952 in order to overcome this ground for rejection, when the allegedly conflicting claims 1-6, 8, 9, 11-17, and 19 are otherwise found to be allowable. Claims 7 and 18 have been cancelled, and therefore the rejection is moot with respect to those claims.

*Double Patenting Rejection #2*

Claims 1-9 and 11-19 are also rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,709,810.

In the interest of expediting prosecution and without acquiescing as to the merits of the rejection, Applicants submit that they will file a terminal disclaimer in the present application to disclaim any term beyond the term of U.S. Patent No. 6,709,810 in order to overcome this ground for rejection, when the allegedly conflicting claims 1-6, 8, 9, 11-17, and 19 are otherwise found to be allowable. Claims 7 and 18 have been cancelled, and therefore the rejection is moot with respect to those claims.

***Claims Rejections under 35 U.S.C. § 112***

*Rejection under 35 U.S.C. § 112, first paragraph*

Claims 1-9 and 11-19 were rejected under 35 U.S.C. § 112, first paragraph, by the Examiner for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claim invention. Applicants respectfully disagree.

The Examiner asserts that the "limitation 'wherein the compound inactivates at least about 1 log of the pathogen' has no support in the originally filed specification" (page 4 of the Office Action).

Applicants contend that the claim element in question does find full support in the originally filed application, including in both the specification and claims of the application as originally filed. Support for the claim element "wherein the compound inactivates at least about 1 log of the pathogen" is found in the specification as originally filed. For instance, support is found in lines 6-11 of paragraph [0086] of page 36 of the specification as originally filed, which indicates that in some embodiments, the pathogen inactivating compounds produce "at least 1 log kill." As indicated in lines 6-7 of paragraph [0031] of page 13 of the specification as originally filed, "1 log kill" means inactivation of pathogens present by 1 log. The element "wherein the compound inactivates at least about 1 log of the pathogen" further finds support in the claims of the application as originally filed. This language was present in claim 1 as filed. Accordingly, nothing in claims 1-

6, 8, 9, 11-17, and 19 is new matter and the inventors clearly had possession of the claimed invention at the time of filing the application.

Claims 7 and 18 have been cancelled, and therefore the rejection is moot with respect to those claims.

Since claims 1-6, 8, 9, 11-17, and 19 are fully supported by the application as originally filed, thereby demonstrating clear possession of the claimed invention at the time of filing, Applicants respectfully request that the rejection of claims 1-6, 8, 9, 11-17, and 19 under 35 U.S.C. § 112, first paragraph, be withdrawn.

*Rejections under 35 U.S.C. § 112, second paragraph*

Claims 1-9 and 11-19 are also rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) The Examiner has indicated that claim 1 is inconsistent in that "no pathogen is required to be present in the material, but the compound is required to inactivate at least about 1 log of the pathogen" (page 5 of the Office Action). The analogous rejection is also applied to claim 9.

Applicants respectfully disagree with the Examiner's assertion that claims 1 and 9 are indefinite. Nevertheless, in the interest of expediting prosecution, Applicants have amended claims 1 and 9 to clearly state that the pathogen that is inactivated is inactivated *if present in the material.*

In light of the amendment of claim 1 and 9, Applicants respectfully request that the rejection of claims 1-6, 8, 9, 11-17, and 19 under 35 U.S.C. § 112, second paragraph be withdrawn.

(2) The Examiner has also noted that claims 4 and 5 are directed to *in vitro* and ex *vivo* methods, respectively, stated that the phrase "*in situ*" in claim 6 is unclear, and requested

clarification or deletion of the phrase. Applicants respectfully contend that the meaning "*in situ*" would not be unclear in the context of the claimed invention to one of ordinary skill in the art. Nevertheless, Applicants offer further clarification as to the meaning of "*in situ*" as follows:

To one of ordinary skill in the art, a "mustard group that is capable of reacting *in situ* to form the electrophilic group" as recited in claim 6 would be readily understood in light of Applicants' specification and claim 1 to refer to a mustard group that is capable of forming the electrophilic group (which can react covalently with nucleic acid) *after* addition to the material comprising red blood cells. For instance, the functional group may be a mustard group that forms a reactive aziridinium ion after addition of the compound containing the mustard group to the material comprising red blood cells. See, e.g., paragraphs [0056]-[0058] and Scheme I on pages 24-26 of Applicants' specification.

With respect to the meanings of "*in vitro*" and "*ex vivo*" as used in claims 4 and 5, the Examiner's attention is directed to paragraphs [0027] and [0028] of Applicants' specification for clarification as to the use of these terms. The "*in vitro*" use of a material or compound is defined in the specification (paragraph 0027]) as a "use of the material or compound outside a living human, mammal, or vertebrate, where the material or compound is not intended for reintroduction into a living human, mammal, or vertebrate." The "*ex vivo*" use of a compound, on the other hand, refers to "using a compound for treatment of a biological material outside a living human, mammal, or vertebrate, where that treated biological material is intended for use inside a living human, mammal, or vertebrate" ([paragraph [0028]).

Although claims 4 and 5 are not limited to methods in which the functional group is a mustard group that is capable of reacting *in situ* to form the electrophilic group, claims 5 and 6 would each encompass such a method. Claim 6 would encompass, but is not limited to, both *in vitro* and *ex vivo* methods in which the functional group is a mustard group that is capable of reacting *in situ* to form the electrophilic group.

In light of the clarification provided above, Applicants respectfully request that this rejection of claim 6 (and of claims 4-5, if also rejected, which was unclear) under 35 U.S.C. § 112, second paragraph be withdrawn.

(3) The Examiner has further indicated that claim 7 should state that the compound "further comprises a nucleic acid binding ligand." The Examiner also indicates that the nucleic acid binding ligand "is an additional group attached the pathogen inactivating moiety [*sic*]."

Claim 7 has been cancelled, and therefore the rejection of claim 7 is moot.

Nevertheless, in light of the amendment of claim 1 to incorporate the elements of claim 7, Applicants wish to point out that, in the method of claim 1, the pathogen-inactivating compound includes, but is *not* limited to, those compounds in which the nucleic acid binding ligand and the functional group, which is, or which forms, an electrophilic group, are two wholly separate moieties linked to each other.

***Claim Rejections under 35 U.S.C. § 102***

*Rejection #1 under 35 U.S.C. § 102*

Claims 1-6 and 11-16 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Roth et al. Applicants respectfully disagree.

To anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Applicants respectfully submit that Roth et al. does not anticipate claims 1-6 and 11-16, because the reference fails to disclose or suggest all elements of the claims. For instance, the method of claim 1, as amended, comprises adding a compound to the material comprising red blood cells that comprises *a nucleic acid binding ligand* and a functional group which is, or which forms, an electrophilic group, wherein the electrophilic group can react covalently with nucleic acid. Nowhere does the Roth et al. reference teach or suggest the use of such a compound in the treatment of red blood cells. Although the Roth et al. reference reports the

use of nitrogen mustard (bis beta chloroethyl-methylamine hydrochloride) as an antisickling agent for the treatment of sickle cell anemia extracorporeally, nitrogen mustard does not comprise a nucleic acid binding ligand.

Since Roth et al. does not teach or suggest each and every element of claims 1-6 and 11-16, Applicants respectfully request that the rejection of claims 1-6 and 11-16 under 35 U.S.C. § 102(b) be withdrawn.

*Rejection #2 under 35 U.S.C. § 102*

Claims 1-9 and 12-19 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by WO 96/14737 or WO 96/39818 or U.S. Patent No. 5,691,132 (the '132 patent) in light of U.S. Patent No. 5,232,844 (the '844 patent). Applicants respectfully disagree.

The methods of claims 1-6, 8, 9, 12-17, and 19 require the addition of an effective amount of a quencher that comprises a nucleophilic group that reacts covalently with the electrophilic group of, or formed by, the pathogen inactivating compound. In addition, the methods of claims 1-6, 8, 9, 12-17, and 19 comprise a step of adding an effective amount of the quencher to the material comprising red blood cells that reduces the level of side reactions of the pathogen-inactivating compound. Claims 7 and 18 are cancelled by this Amendment, and therefore the rejection is moot with respect to those claims.

As noted above, to anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Applicants respectfully submit that the cited references do not anticipate claims 1-6, 8, 9, 12-17, and 19, because the references fail to disclose or suggest all elements of the claims.

In the Office Action, the Examiner cites references that teach the treatment of red blood cell compositions with quinacrine mustard in the presence of solutions containing Adsol and, referencing the '844 patent, asserts that mannitol, a component of Adsol, is a "well known quencher." Applicants contend that even if mannitol acts as a quencher with respect to the

compounds and/or chemical reactions that are taught in the '844 patent, mannitol would *not* be considered to be a quencher of the pathogen-inactivating compounds in either Applicants' claimed methods or in the cited disclosures of WO 96/14737, WO 96/39818, and the '132 patent. Instead, one of ordinary skill in the art would recognize the mannitol-containing Adsol as being a well-known preservative for red blood cells and merely being used as such in WO 96/14737, WO 96/39818, the '132 patent, and Applicants' specification.

The '844 patent cited by the Examiner as characterizing mannitol as a quencher relates to the use of *photoreactive* compounds, such as phthalocyanines, to inactivate viruses in biological compositions. This is evident throughout the specification and claims of the '844 patent. See, e.g., the title ("Photodynamic Inactivation of Viruses in Cell-Containing Compositions"), the abstract which indicates the methods of the '844 patent comprise contacting the compositions with "a virucidally effective amount of at least one photoreactive compound," lines 6-41 of column 5, lines 52-58 of column 6, and line 29 of column 7 to line 15 of column 8, of the '844 patent. Accordingly, compounds which are suitable for quenching the reactions of photoreactive compounds or their products are labeled as "quenchers" in the '844 patent. The '844 patent states that for the methods of that particular patent "suitable quenchers are any substances known to react with free radicals or reactive forms of oxygen, more specifically which decrease the efficiencies of photodynamically catalyzed chemical reactions (e.g., DNA strand breads [*sic*]), or decrease the cytotoxicity in photodynamic cell killing experiments" (column 8, lines 7-15 of the '844 patent). The next paragraph in the '844 patent, cited by the Examiner, merely indicates that mannitol is a representative quencher for those photoreactive compounds used in the methods of the '844 patent.

The chemistry of quinacrine mustard and the other pathogen-inactivating compounds taught in Applicants' specification is very different from the photoactivated pathogen inactivators taught in the '844 patent. The quinacrine mustard pathogen inactivating compound described in the cited references WO 96/14737, WO 96/39818 and the '132 patent, as well as in Applicants' specification, differs from the reagents used in the '844 patent in that quinacrine mustard does not require photoactivation to inactivate pathogens. See, e.g., paragraph [0007], pages 2-3, of Applicants' specification. Rather, quinacrine mustard generates a reactive electrophile *in situ* that

can react covalently with nucleic acid. Applicants' specification also states that the ideal pathogen-inactivating compounds "react with pathogens by an electrophilic process, and do not require photoactivation" (lines 4-5 of paragraph [0008], page 3). Furthermore, as indicated in lines 5-6 of paragraph [0008], page 3, of Applicants' specification, "reactive oxygen or free radical species are not produced, and oxidative damage is not a concern." In addition, the language of claim 1 clearly states that the compound added to inactivate the pathogen comprises a "functional group which is, or which forms, an electrophilic group, wherein the electrophilic group can react covalently with nucleic acid."

Since quinacrine mustard does not require photoactivation to inactivate pathogens, suitable quenchers for quinacrine mustard do not necessarily include "substances known to react with free radicals or reactive forms of oxygen," such as mannitol, but rather would be expected to be compounds that comprise nucleophilic groups that can react covalently with the aziridinium ion formed by the quinacrine mustard *in situ*. Furthermore, claim 1 indicates that, in the claimed methods, the added quencher comprises a nucleophilic group that reacts covalently with the electrophilic group of, or formed by, the pathogen-inactivating compound in the material comprising red blood cells. Nothing in the '844 patent or the other references cited by the Examiner remotely teaches or suggests that mannitol would function as a nucleophile reactive with and/or quench quinacrine mustard or the other pathogen-inactivating compounds of Applicants' claimed methods which comprise a functional group which is, or which forms, an electrophilic group that can react covalently with nucleic acid in a red blood cell composition.

In addition, claim 1 states that an effective amount of the quencher is added that "reduces the level of side reactions of the compound in the material comprising red blood cells." Nothing in the '844 patent or the other references cited by the Examiner remotely teaches or suggests that the mannitol in Adsol "reduces the level of side reactions of" quinacrine mustard in a red blood cell composition in those references.

In fact, Applicants' own data as reported in the specification demonstrates that the mannitol in Adsol is *not* an effective nucleophilic quencher in red blood cell compositions for a

pathogen-inactivating compound, PIC-1, which, like quinacrine mustard, comprises a mustard. (The structure of PIC-1 is found in paragraph [0039] of Applicants' specification.) Adsol is present in each of the 16 samples comprising red blood cells used in the study in Example 9. See paragraph [00124] on page 51. The pathogen-inactivating compound PIC-1 was added to most of the samples after glutathione, cysteine, or no quencher was added. After the treatment, aliquots of the diluted, washed red blood cells were incubated with anti-human IgG, anti-human albumin, or anti-acridine antibodies to assess the level of undesired side reactions caused by PIC-1 in the reaction mixtures.

Results for each of the samples in the experiments of Example 9 are shown in Table 9 on page 53. Sample #2 in Table 9 was treated with PIC-1 in the presence of the Adsol, but with no glutathione or cysteine added. Since no PIC-1 was added to samples #1, 3, and 10, the red blood cells in those samples were free of side reactions due to PIC-1. The high amounts of antibody binding shown by the high values in the last three columns of Table 9 for sample #2 relative to the low amounts of antibody binding shown by the low values in the last three columns for samples #1, 3, and 10 in which no PIC-1 was added (and therefore no PIC-1 side reactions occurred), indicate that a very measurable amount of side reactions due to PIC-1 occurred in sample #2 *despite the fact that Adsol was present in sample #2*. By contrast, in those samples in which the true quenchers glutathione and cysteine function were added (samples 4-9 and 11-16), the level of side reactions caused by the PIC-1 decreased as evidenced by the decreased antibody binding levels relative to sample #2. Furthermore, larger amounts of the quenchers glutathione or cysteine brought the levels of antibody binding down to levels near those of the "no PIC-1" controls (samples #1, 3, and 10) which represent the levels expected when no PIC-1 side reactions occur. Thus, the results of Example 9 indicate that glutathione and cysteine function as effective quenchers for the mustard-containing pathogen inactivating compound PIC-1, whereas the mannitol in Adsol does not.

Since WO 96/14737, WO 96/39818 and the '132 patent, in light of the '844 patent do not teach or suggest each and every element of claims 1-6, 8, 9, 12-17, and 19, Applicants respectfully request that the rejection of claims 1-6, 8, 9, 12-17, and 19 under 35 U.S.C. § 102(b) be withdrawn.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 282172000602. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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